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<i>2/52</i> <i>Fig.1(i)</i>	<i>3/52</i> <i>Fig.1(ii)</i>
<i>4/52</i> <i>Fig.1(iii)</i>	<i>5/52</i> <i>Fig.1(iv)</i>

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1	TCGGCCTCC GAAACC ATG AAC TTT CTG	
	Met Asn Phe Leu	1
50	CTT GCC TTG CTG CTC TAC CTC CAC	
	Leu Ala Leu Leu Leu Tyr Leu His	15
98	CCC ATG GCA GAA GGA GGA GGG CAG	
	Pro Met Ala Glu Gly Gly Gly Gln	30 35
146	ATG GAT GTC TAT CAG CGC AGC TAC	
	Met Asp Val Tyr Gln Arg Ser Tyr	45 50
194	GAC ATC TTC CAG GAG TAC CCT GAT	
	Asp Ile Phe Gln Glu Tyr Pro Asp	60 65
242	TCC TGT GTG CCC CTG ATG CGA TGC	
	Ser Cys Val Pro Leu Met Arg Cys	80
290	CTC GAG TGT GTG CCC ACT GAG GAG	
	Leu Glu Cys Val Pro Thr Glu Glu	95
338	CGG ATC AAA CCT CAC CAA GGC CAG	
	Arg Ily Lys Pro His Gln Gly Gln	110 115

Fig.1(i)

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CTG	TCT	TGG	GTG	CAT	TGG	AGC		49
Leu	Ser	Trp	Val	His	Trp	Ser		
5					10			
CAT	GCC	AAG	TGG	TCC	CAG	GCT	GCA	97
His	Ala	Lys	Trp	Ser	Gln	Ala	Ala	
20					25			
AAT	CAT	CAC	GAA	GTG	GTG	AAG	TTC	145
Asn	His	His	Glu	Val	Val	Lys	Phe	
				40				
TGC	CAT	CCA	ATC	GAG	ACC	CTG	GTG	193
Cys	His	Pro	Ile	Glu	Thr	Leu	Val	
			55					
GAG	ATC	GAG	TAC	ATC	TTC	AAG	CCA	241
Glu	Ile	Glu	Tyr	Ile	Phe	Lys	Pro	
		70					75	
GGG	GGC	TGC	TGC	AAT	GAC	GAG	GGC	289
Gly	Gly	Cys	Cys	Asn	Asp	Glu	Gly	
	85					90		
TCC	AAC	ATC	ACC	ATG	CAG	ATT	ATG	337
Ser	Asn	Ile	Thr	Met	Gln	Ile	Met	
100					105			
CAC	ATA	GGA	GAG	ATG	AGC	TTC	CTA	385
His	Ile	Gly	Glu	Met	Ser	Phe	Leu	
			120					

Fig.1(ii)

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386	CAG CAC AAC AAA TGT GAA TGC AGA
	Gln His Asn Lys Cys Glu Cys Arg
	125 130
434	GAA AAT CCC TGT GGG CCT TGC TCA
	Glu Asn Pro Cys Gly Pro Cys Ser
	140 145
482	CAA GAT CCG CAG ACG TGT AAA TGT
	Gln Asp Pro Gln Thr Cys Lys Cys
	160
530	TGC AAG GCG AGG CAG CTT GAG TTA
	Cys Lys Ala Arg Gln Leu Glu Leu
	175
578	AAG CCG AGG CGG TGAGCCGGGC AGGAG
	Lys Pro Arg Arg
	190
630	GAACCAGATC TCTCACCAGG

Fig.1(iii)

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CCA AAG AAA GAT AGA GCA AGA CAA	433
Pro Lys Lys Asp Arg Ala Arg Gln	
135	
GAG CGG AGA AAG CAT TTG TTT GTA	481
Glu Arg Arg Lys His Leu Phe Val	
150 155	
TCC TGC AAA AAC ACA GAC TCG CGT	529
Ser Cys Lys Asn Thr Asp Ser Arg	
165 170	
AAC GAA CGT ACT TGC AGA TGT GAC	577
Asn Glu Arg Thr Cys Arg Cys Asp	
180 185	
GAAGG AGCCTCCCTC AGCGTTTCGG	629

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Fig.1(iv)

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7/52 Fig. 2(i)	8/52 Fig. 2(ii)
9/52 Fig 2(iii)	10/52 Fig 2(iv)
11/52 Fig 2(v)	12/52 Fig 2(vi)

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1	CC ATG AGC CCT CTG CTC CGC CGC Met Ser Pro Leu Leu Arg Arg 1 5
48	CTG GCC CCC GCC CAG GCC CCT GTC Leu Ala Pro Ala Gln Ala Pro Val 20
96	CAG AGG AAA GTG GTG TCA TGG ATA Gln Arg Lys Val Val Ser Trp Ile 35
144	CAG CCC CGG GAG GTG GTG GTG CCC Gln Pro Arg Glu Val Val Val Pro 50 55
192	GTG GCC AAA CAG CTG GTG CCC AGC Val Ala Lys Gln Leu Val Pro Ser 65 70
240	GGC TGC TGC CCT GAC GAT GGC CTG Gly Cys Cys Pro Asp Asp Gly Leu 80 85
288	CAA GTC CGG ATG CAG ATC CTC ATG Gln Val Arg Met Gln Ile Leu Met 100
336	GGG GAG ATG TCC CTG GAA GAA CAC Gly Glu Met Ser Leu Glu Glu His 115

Fig.2(i)

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CTG	CTG	CTC	GCC	GCA	CTC	CTG	CAG	47
Leu	Leu	Leu	Ala	Ala	Leu	Leu	Gln	
		10					15	
TCC	CAG	CCT	GAT	GCC	CCT	GGC	CAC	95
Ser	Gln	Pro	Asp	Ala	Pro	Gly	His	
	25					30		
GAT	GTG	TAT	ACT	CGC	GCT	ACC	TGC	143
Asp	Val	Tyr	Thr	Arg	Ala	Thr	Cys	
	40				45			
TTG	ACT	GTG	GAG	CTC	ATG	GGC	ACC	191
Leu	Thr	Val	Glu	Leu	Met	Gly	Thr	
			60					
TGC	GTG	ACT	GTG	CAG	CGC	TGT	GGT	239
Cys	Val	Thr	Val	Gln	Arg	Cys	Gly	
			75					
GAG	TGT	GTG	CCC	ACT	GGG	CAG	CAC	287
Glu	Cys	Val	Pro	Thr	Gly	Gln	His	
		90					95	
ATC	CGG	TAC	CCG	AGC	AGT	CAG	CTG	335
Ile	Arg	Tyr	Pro	Ser	Ser	Gln	Leu	
	105					110		
AGC	CAG	TGT	GAA	TGC	AGA	CCT	AAA	383
Ser	Gln	Cys	Glu	Cys	Arg	Pro	Lys	
120					125			

Fig. 2(ii)

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384	AAA	AAG	GAC	AGT	GCT	GTG	AAG	CCA
	Lys	Lys	Asp	Ser	Ala	Val	Lys	Pro
			130					135
432	CGT	CCC	CAG	CCC	CGT	TCT	GTT	CCG
	Arg	Pro	Gln	Pro	Arg	Ser	Val	Pro
		145					150	
480	CCC	TCC	CCA	GCT	GAC	ATC	ACC	CAT
	Pro	Ser	Pro	Ala	Asp	Ile	Thr	His
	160					165		
528	GCC	CAC	GCT	GCA	CCC	AGC	ACC	ACC
	Ala	His	Ala	Ala	Pro	Ser	Thr	Thr
					180			
576	GCT	GCC	GCT	GCC	GAC	GCC	GCA	GCT
	Ala	Ala	Ala	Ala	Asp	Ala	Ala	Ala
				195				

Fig. 2(iii)

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GAC	AGG	GCT	GCC	ACT	CCC	CAC	CAC	431
Asp	Arg	Ala	Ala	Thr	Pro	His	His	
				140				
GGC	TGG	GAC	TCT	GCC	CCC	GGA	GCA	479
Gly	Trp	Asp	Ser	Ala	Pro	Gly	Ala	
				155				
CCC	ACT	CCA	GCC	CCA	GGC	CCC	TCT	527
Pro	Thr	Pro	Ala	Pro	Gly	Pro	Ser	
			170				175	
AGC	GCC	CTG	ACC	CCC	GGA	CCT	GCC	575
Ser	Ala	Leu	Thr	Pro	Gly	Pro	Ala	
			185				190	
TCC	TCC	GTT	GCC	AAG	GGC	GGG	GCT	T 624
Ser	Ser	Val	Ala	Lys	Gly	Gly	Ala	
200					205			

Fig.2(iv)

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625 AGAGCTCAAC CCAGACACCT GCAGGTGCCG
685 GACTCAGCAG GGTGACTTGC CTCAGAGGCT
745 GGTAATAAAC AGCCAAGCCC CCAAGACCTC
805 GCCTCTCAGA GGGCTCTTCT GCCATCCCTT
865 GAGTTGGAAG AGGAGACTGG GAGGCAGCAA
825 GGAGTACTGT CTCAGTTTCT AACCACTCTG
985 CTCCCCTCAC TAAGAAGACC CAAACCTCTG
1045 CTGTGACCCC CAACCCTGAT AAAAGAGATG

Fig.2(v)

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GAAGCTGCGA	AGGTGACACA	TGGCTTTTCA	684
ATATCCCAGT	GGGGGAACAA	AGGGGAGCCT	744
AGCCCAGGCA	GAAGCTGCTC	TAGGACCTGG	804
GTCTCCCTGA	GGCCATCATC	AAACAGGACA	864
GAGGGGTCAC	ATACCAGCTC	AGGGGAGAAT	924
TGCAAGTAAG	CATCTTACAA	CTGGCTCTTC	984
CATAATGGGA	TTTGGGCTTT	GGTACAAGAA	1044
GAAGGAAAAA	AAAAAAAAAA		1094

Fig.2(vi)

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14/52	15/52
Fig.3(i)	Fig.3(ii)

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```
>VEGF_HUMAN VEGF_HUMAN VASCULAR ENDOTHELIAL
      (VASCULAR 215 AA.
      LENGTH = 215
```

SCORE = 181 (92.4 BITS), EXPECT = 6.4e-20,
IDENTITIES = 33/75 (44%), POSITIVES = 48/75

```

QUERY:      31 HQRKVVSIDVYTRATCQPREVVVPLTVEL
              +++ VV +DVY R+ C+P E +V + E
SUBJCT:     36 NHHEVVKFMDVYQRSYCHPIETLVDIFQEY

```

QUERY: 91 PTGQHQVRMQILMIR 105
PT + + MQI+ I+
SBJCT: 96 PTEESNITMQIMRIK 110

SCORE = 76 (38.8 BITS), EXPECT = 0.0011,
IDENTITIES = 12/19 (63%), POSITIVES = 16/19

```

QUERY:      110  QLGEMSLEEHSQCECRPKK 128
              ++GEMS  +H+  CECRPKK
SBJCT:      116  HIGEMSFLQH NKCECRPKK 134

```

SCORE = 72 (36.8 BITS), EXPECT = 0.0046,
IDENTITIES = 14/21 (66%), POSITIVES = 15/21

QUERY: 202 RCQGRGLELNPDTCRCKLRR 222
 RC +R LELN TCRC K RR
 SBJCT: 195 RCKARQLELNERTCRCDKPRR 215

SCORE = 46 (23.5 BITS), EXPECT = 47.,
IDENTITIES = 6/10 (60%), POSITIVES = 9/10

```

QUERY:      187 DPRTCRCRCR 196
              DP+TC+C C+
SBJCT:      181 DPQTCKCSCK 190

```

SUBSTITUTE SHEET (RULE 26)

Fig.3(i)

Variable	Group 1		Group 2		Group 3		Group 4		Group 5		Group 6		Group 7		Group 8		Group 9		Group 10			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Age	25.5	2.5	26.0	2.5	26.5	2.5	27.0	2.5	27.5	2.5	28.0	2.5	28.5	2.5	29.0	2.5	29.5	2.5	30.0	2.5	30.5	2.5
Height	170.0	5.0	171.0	5.0	172.0	5.0	173.0	5.0	174.0	5.0	175.0	5.0	176.0	5.0	177.0	5.0	178.0	5.0	179.0	5.0	180.0	5.0
Weight	70.0	10.0	71.0	10.0	72.0	10.0	73.0	10.0	74.0	10.0	75.0	10.0	76.0	10.0	77.0	10.0	78.0	10.0	79.0	10.0	80.0	10.0
Heart rate	72.0	10.0	73.0	10.0	74.0	10.0	75.0	10.0	76.0	10.0	77.0	10.0	78.0	10.0	79.0	10.0	80.0	10.0	81.0	10.0	82.0	10.0
Blood pressure	120/80	10/5	121/81	10/5	122/82	10/5	123/83	10/5	124/84	10/5	125/85	10/5	126/86	10/5	127/87	10/5	128/88	10/5	129/89	10/5	130/90	10/5
Respiratory rate	12.0	2.0	12.5	2.0	13.0	2.0	13.5	2.0	14.0	2.0	14.5	2.0	15.0	2.0	15.5	2.0	16.0	2.0	16.5	2.0	17.0	2.0
SpO2	98.0	1.0	98.5	1.0	99.0	1.0	99.5	1.0	100.0	1.0	100.0	1.0	100.0	1.0	100.0	1.0	100.0	1.0	100.0	1.0	100.0	1.0
ECG	Normal		Normal		Normal		Normal		Normal		Normal		Normal		Normal		Normal		Normal		Normal	
Lab tests	Normal		Normal		Normal		Normal		Normal		Normal		Normal		Normal		Normal		Normal		Normal	
Immunization	Up to date		Up to date		Up to date		Up to date		Up to date		Up to date		Up to date		Up to date		Up to date		Up to date		Up to date	
Family history	No		No		No		No		No		No		No		No		No		No		No	
Personal history	No		No		No		No		No		No		No		No		No		No		No	
Medication	No		No		No		No		No		No		No		No		No		No		No	
Social history	No		No		No		No		No		No		No		No		No		No		No	
Review of systems	No		No		No		No		No		No		No		No		No		No		No	
Physical examination	No		No		No		No		No		No		No		No		No		No		No	
Diagnosis	No		No		No		No		No		No		No		No		No		No		No	
Prognosis	No		No		No		No		No		No		No		No		No		No		No	
Treatment	No		No		No		No		No		No		No		No		No		No		No	
Follow-up	No		No		No		No		No		No		No		No		No		No		No	
Discharge	No		No		No		No		No		No		No		No		No		No		No	
Referral	No		No		No		No		No		No		No		No		No		No		No	
Admission	No		No		No		No		No													

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GROWTH FACTOR PRECURSOR (VEGF)

 $P = 6.4e-20$
(64%) $MGTVAKQLVPSCVTVQRCGGCCPDDGLECV$ 90
+ $PSCV + RCGGCC D+GLECV$
 $PDEIEYIFKPSCVPLMRCGGCCNDEGLECV$ 95POISSON $P(2) = 9.1e-12$
(84%)POISSON $P(3) = 3.6e-18$
(71%)POISSON $P(4) = 7.3e-10$
(90%)*Fig. 3(i)*

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17/52 Fig. 4(i)	18/52 Fig. 4(ii)
19/52 Fig. 4(iii)	20/52 Fig. 4(iv)

18/52

TGCTCGCCGCACT.....CC	67
...TGGGTGCATTGGAGCCTTGCCT	56
 TGCTCTCCAGCCTGATGCCCCTGGC	117
GTGGTCCCAGGCTGCA.CCCATGGC	105
 .AAGTGGTG....TCATGGATAGAT	147
GAAGTGGTGAAGTTCATG....GAT	151
 CCCCGGGAG...GTGGTGGTGCCCT	193
CCAATCGAGACCCTGGTGGACATCT	200
 GGGCACCGTGGCCAAACAGCTGGTG	234
GTACATCTT...CAA.....G	238
 GTGGTGGCTGCTGCCCTGACGATGG	284
GCGGGGGCTGCTGCAATGACGAGGG	288
 CACCAAGTCCGGATGCAGAT.....	329
TCCAACATCACCATGCAGATTATGC	338

Fig.4(ii)

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Gap Weight:3.00 Average Match:1.000
 Length Weight:0.100 Average Mismatch:-0.900
 Quality:100.9 Length:739
 Ratio:0.175 Gaps:30
 Percent Percent
 Similarity:69.703 Identity:69.703

```

28   ATGAGCCCTCTGCTCCGCCGCCTGC
    |||| | ||||| | ||
17   ATGAACTTTCTGCT.....GTCT..

68   TGCAGCTGGCCCCCGCCCAGGCCCC
    ||| ||| || | ||| |||
57   TGCTGCTCTACCTCCACCATGCCAA

118  CACCAGAGGA.....
      |||||
106  AGAAGGAGGAGGGCAGAATCATCAC

140  GTGTATACTCGC.GCTACCTGCCAG
    || ||| ||| |||| |||||
152  GTCTATCAGCGCAGCTA.CTGCCAT

194  T....GA.....CTGTGGAGCTCAT
    | || ||| ||| ||
201  TCCAGGAGTACCCTGATGAGATCGA

235  CCCAGCTGCGTGACTGTGCAGCGCT
    || ||| ||| | || |||
239  CCATCCTGTGTGCCCCTGATGCGAT

285  CCTGGAGTGTGTGCCCCACTGGGCAG
    ||||| ||||| ||||| |||
289  CCTGGAGTGTGTGCCCCACTGAGGAG
  
```

Fig.4(i)

SUBSTITUTE SHEET (Rule 26)

19/52

330CCTCATGATCCGGTACC
 |||||
339 GGATCAAACCTCA.....C

369 GTCCCTGGAAGAACACAGCCAGTGT
 | | | | | | | | | | | | |
376 GAGCTTCCTACAGCACAAACAAATGT

419 GTGCTGTGAAGCCAGACAGGGCTGC
 | ||| ||||| |
423 G.....AGCAAGACAAG.....

469 CGTTCTGTTCCGGGCTGGGACTCTG
 | | | | | | | | |
443 ...TGTGGGCCTTGCTCAGA.....

519 CATCACCCATCCCACTCCAGCCCCA

468

569 GC.....ACCACCAGCGCCC
 || |||
469 GCATTGTGTTGTACAA.....

609 TGCCGACGCCGCAGCTTCCTCCGTT
 || | | | | | | | | | | |
509 TG.CAAAAACACAGACTC..GCGTT

657 AACCCAGACACCTGCAGGTGCCGGA
 ||| |
554 AACGAACGTACTTGCAGATGTGACA

Fig.4(iii)

20/52

CGAGCAGTCAGC...TGGGGGAGAT	368
CAAG...GCCAGCACATAGGAGAGAT	375
GAATGCAGACCTAAAAAAAGGACA	418
GAATGCAGACC...AAAGAAAGATA	422
CACTCCCCACCACCGTCCCCAGCCC	468
.....AAAATCCC.....	442
CCCCCGGAGCACCTCCCCAGCTGA	518
...GCGGAGAA.....	467
GGCCCCTCTGCCCACGCTGCACCCA	568
.....A	468
TGACCCCCGGACCTGCCGCTGCCGC	608
.GATCCGCAGACGTGTAAATGTTCC	508
GCCAAGGGCGGGGC..TTAGAGCTC	656
GC..AAGGCGAGGCAGCTTGAGTTA	553
AGCTGCGAAGGTGA	695
AGCCGAGGCGGTGA	592

Fig.4(iv)

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22/52 [*] <i>Fig. 5(i)</i>	23/52 <i>Fig. 5(ii)</i>	24/52 <i>Fig. 5(iii)</i>
25/52 <i>Fig. 5(iv)</i>	26/52 <i>Fig. 5(v)</i>	27/52 <i>Fig. 5(vi)</i>

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165SOMSQ.MSF.msf MSF:687

Type: D Tuesday, June 20, 1995

Check:3140

	1
VEGF165	ATGAACTTTCTGCTGTCTTGGGTG
SOM175	ATGAGCCCTCTGCTCCGCCGCCTG
SOM175-e6	ATGAGCCCTCTGCTCCGCCGCCTG
SOM175-e6&7	ATGAGCCCTCTGCTCCGCCGCCTG
SOM175-e4	ATGAGCCCTCTGCTCCGCCGCCTG
	81
VEGF165	CACCCATGGCAGAAGGAGGAGGGC
SOM175	TGCCCCTGGCCACCAGAGGAAAGT
SOM175-e6	TGCCCCTGGCCACCAGAGGAAAGT
SOM175-e6&7	TGCCCCTGGCCACCAGAGGAAAGT
SOM175-e4	TGCCCCTGGCCACCAGAGGAAAGT
	161
VEGF165	CCAATCGAGACCCTGGTGGACATC
SOM175	GTGGTGGTGCCCTTGACTG.TGGA
SOM175-e6	GTGGTGGTGCCCTTGACTG.TGGA
SOM175-e6&7	GTGGTGGTGCCCTTGACTG.TGGA
SOM175-e4	GTGGTGGTGCCCTTGACTG.TGGA
	241
VEGF165	GATGCGATGCGGGGGCTGCTGCAA
SOM175	GCAGCGCTGTGGTGGCTGCTGCCC
SOM175-e6	GCAGCGCTGTGGTGGCTGCTGCCC
SOM175-e6&7	GCAGCGCTGTGGTGGCTGCTGCCC
SOM175-e4	GCAGCGCTGTGGTGGCTGCTGCCC

Fig.5(i)

SUBSTITUTE SHEET (RULE 26)

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CATTGGAGCCTTGCCTTGCTGCTCTACC
CTGCTCGCCGCACTCCTGCAGCTGGCCC
CTGCTCGCCGCACTCCTGCAGCTGGCCC
CTGCTCGCCGCACTCCTGCAGCTGGCCC
CTGCTCGCCGCACTCCTGCAGCTGGCCC

AGAATCATCACGAAGTGGTGAAGTTCAT
GGTGTTCATGGATAGATGTGTATACTCGC
GGTGTTCATGGATAGATGTGTATACTCGC
GGTGTTCATGGATAGATGTGTATACTCGC
GGTGTTCATGGATAGATGTGTATACTCGC

TTCCAGGAGTACCCTGATGAGATCGAGT
GCTCATGGGCACCGTGGCCAAAC..AGC
GCTCATGGGCACCGTGGCCAAAC..AGC
GCTCATGGGCACCGTGGCCAAAC..AGC
GCTCATGGGCACCGTGGCCAAAC..AGC

TGACGAGGGCCTGGAGTGTGTGCCCCACT
TGACGATGGCCTGGAGTGTGTGCCCCACT
TGACGATGGCCTGGAGTGTGTGCCCCACT
TGACGATGGCCTGGAGTGTGTGCCCCACT
TGACGATGGCCTGGAGTGTGTGCCCCACT

Fig.5(ii)

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80

TCCACCATGCCAAGTGGTCCCAGGCTG.
CCGCCCAGGCCCCTGTCTCCCAGCCTGA
CCGCCCAGGCCCCTGTCTCCCAGCCTGA
CCGCCCAGGCCCCTGTCTCCCAGCCTGA
CCGCCCAGGCCCCTGTCTCCCAGCCTGA

160

GGATGTCTATCAGCGCAGCTACTGCCAT
G.....CTACCTGC.CAGCC.CCGGGAG
G.....CTACCTGC.CAGCC.CCGGGAG
G.....CTACCTGC.CAGCC.CCGGGAG
G.....CTACCTGC.CAGCC.CCGGGAG

240

ACATCTTCAAGCCATCCTGTGTGCCCCCT
TGGTGCCCAG.....CTGCGTGACTGT
TGGTGCCCAG.....CTGCGTGACTGT
TGGTGCCCAG.....CTGCGTGACTGT
TGGTGCCCAG.....CTGCGTGACTGT

320

GAGGAGTCCAACATCACCATGCAGATTA
GGGCAGCACCAAGTCCGGATGCAGATCC
GGGCAGCACCAAGTCCGGATGCAGATCC
GGGCAGCACCAAGTCCGGATGCAGATCC
GGGCAGCACCAAGTCCGGATGCAGA...

Fig.5(iii)

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321
VEGF165 TGCGGATCAAACCTCACCAAGGCC
SOM175 TCATGATCCGG...TACCCGAGCA
SOM175-e6 TCATGATCCGG...TACCCGAGCA
SOM175-e6&7 TCATGATCCGG...TACCCGAGCA
SOM175-e4

401
VEGF165 AAGAAAGATAG.....AGCAA
SOM175 AAAAAGGACAGTGCTGTGAAGCCA
SOM175-e6 AAAAAGGACAGTGCTGTGAAGCCA
SOM175-e6&7 AAAAAGGACAGTGCTGTGAAGCCA
SOM175-e4 AAAAAGGACAGTGCTGTGAAGCCA

481
VEGF165AAGCA.....
SOM175 CTCTGCCCCCGGAGCACCCCTCCCC
SOM175-e6
SOM175-e6&7
SOM175-e4 CTCTGCCCCCGGAGCACCCCTCCCC

561
VEGF165 A.....GATCCGCA
SOM175 GCACCACCAGCGCCCTGACCCCCG
SOM175-E6 GCACCACCAGCGCCCTGACCCCCG
SOM175-e6&7
SOM175-e4 GCACCACCAGCGCCCTGACCCCCG

641
VEGF165 TTGAGTTAAACGAACGTACTTGCA
SOM175 TAGAGCTCAACCCAGACACCTGCA
SOM175-e6 TAGAGCTCAACCCAGACACCTGCA
SOM175-e6&7
SOM175-e4 TAGAGCTCAACCCAGACACCTGCA

Fig.5(iv)

Fig.5(iv)

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AGCACATAGGAGAGATGAGCTTCCTACA
GTCAGCTGGGGGAGATGTCCCTGGAAGA
GTCAGCTGGGGGAGATGTCCCTGGAAGA
GTCAGCTGGGGGAGATGTCCCTGGAAGA
.....

GACAAGAA....AATCCCTGTGG.....
GACAGGGCTGCCACTCCCCACCACCGTC
GATAG.....
GATAG.....
GACAGGGCTGCCACTCCCCACCACCGTC

.....
AGCTGACATCACCCATCCCACTCCAGCC
.....CC
.....
AGCTGACATCACCCATCCCACTCCAGCC

GACGTGTAAATGTTCTGCAAAAAC.AC
GACCTGCCGCTGCCGCTGCCGACGCCGC
GACCTGCCGCTGCCGCTGCCGACGCCGC
.....
GACCTGCCGCTGCCGCTGCCGACGCCGC

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GATGTGACAAGCCGAGGCGGTGA
GGTGCCGGAAGCTGCGAAGGTGA
GGTGCCGGAAGCTGCGAAGGTGA
.GTGCCGGAAGCTGCGAAGGTGA
GGTGCCGGAAGCTGCGAAGGTGA

Fig.5(v)

T02F0202060

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400

GCACAACAAATGTGAATGCAGACC...A
ACACAGCCAGTGTGAATGCAGACCTAAA
ACACAGCCAGTGTGAATGCAGACCTAAA
ACACAGCCAGTGTGAATGCAGACCTAAA
.....CCTAAA

480

.....GCCTTGCTCAGAGCGGAGA
CCCAGCCCCGTTCTGTTCCGGGCTGGGA
.....
.....
CCCAGCCCCGTTCTGTTCCGGGCTGGGA

560

.....TTTGTT.....TGTAC..A
CCAGGCCCCCTCTGCCCACGCTGCACCCA
CCAGGCCCCCTCTGCCCACGCTGCACCCA
.....
CCAGGCCCCCTCTGCCCACGCTGCACCCA

640

AGACTCG..CGTTGCAAGGCGAGGCAGC
AGCTTCCTCCGTTGCCAAGGGCGGGGCT
AGCTTCCTCCGTTGCCAAGGGCGGGGCT
.....
AGCTTCCTCCGTTGCCAAGGGCGGGGCT

Fig.5(vi)

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<i>Fig 6(i)</i>	29/52	<i>Fig 6(ii)</i>	30/52
<i>Fig 6(iii)</i>	31/52		

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VEGF ₁₆₅	M	N	F	L	L	S	W	V	H	W	S	L	A	L	A	L	L	Y	L	H	H	A	K	W	S	Q	A	A	P
SOM175 _{Short}	M	S	P	L	L	R	R	L	L	.	.	L	A	L	A	L	L	Q	L	A	P	A	Q	A	P
VEGF ₁₆₅	I	F	Q	E	Y	P	D	E	I	E	Y	I	F	K	P	S	C	V	P	L	M	R	C	G	G	C	C	N	
SOM175 _{Short}	L	T	V	E	L	M	G	T	V	A	K	Q	L	V	P	S	C	V	T	V	Q	R	C	G	G	C	C	P	
VEGF ₁₆₅	F	L	Q	H	N	K	C	E	C	R	P	K	K	D	R	A	
SOM175 _{Short}	L	E	E	H	S	Q	C	E	C	R	P	K	K	K	D	S	A	V	K	P	D	R	A	A	T	P	H		
VEGF ₁₆₅	C	K	C	S	C	K	N	T	D	S	R	C	K	A	R	Q	L	E	L	N	E	R	T	C	R	C	D	K	
SOM175 _{Short}	H	A	A	P	S	T	S	A	L	T	P	G	P	A	A	A	A	A	A	D	A	A	S	S	V	A	K		
OR...																													
VEGF ₁₆₅	M	N	F	L	L	S	W	V	H	W	S	L	A	L	A	L	L	Y	L	H	H	A	K	W	S	Q	A	A	P
SOM175 _{Long}	M	S	P	L	L	R	R	L	L	.	.	L	A	L	A	L	L	Q	L	A	P	A	Q	A	P
VEGF ₁₆₅	I	F	Q	E	Y	P	D	E	I	E	Y	I	F	K	P	S	C	V	P	L	M	R	C	G	G	C	C	N	
SOM175 _{Long}	L	T	V	E	L	M	G	T	V	A	K	Q	L	V	P	S	C	V	T	V	Q	R	C	G	G	C	C	P	
VEGF ₁₆₅	F	L	Q	H	N	K	C	E	C	R	P	K	K	D	R	A	
SOM175 _{Long}	L	E	E	H	S	Q	C	E	C	R	P	K	K	K	D	S	A	V	K	P	D	R	A	A	T	P	H		
VEGF ₁₆₅	G	P	C	S	E	R	R	K	H	L	F	V	Q	D	P	Q	T	C	K	C	S	C	K	N	T	D	S	.	
SOM175 _{Long}	P	R	C	T	Q	H	H	Q	R	.	.	P	D	D	P	R	T	C	R	C	R	C	R	R	R	S	F	L	

Fig.6(ii)

Fig.6(i)

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M A E G G G Q N	H H E	V V	K F M	D V Y	Q R S	Y C H	P I E	T L V	D	60
V S Q P D A P G H	Q R K	V V	S W I	D V Y	T R A	T C C	P R E	V V V	P	55
D E G L E C V P T	E E S N I	T M Q	I M R	I K P	H Q G	Q H I	G E M S		121	
D D G L E C V P T	G Q H Q V	R M Q	I L M	I R	Y P S	S Q L	G E M S		115	
· · · · ·	R Q E N	P C G	P C S E R R K	H L F	· V Q D	P Q T		170		
R P Q P R S V P G W D S A	P G A	P S P A D I T H				P S A	175			
P R R									191	
G G A									207	
M A E G G G Q N	H H E	V V	K F M	D V Y	Q R S	Y C H	P I E	T L V	D	60
V S Q P D A P G H	Q R K	V V	S W I	D V Y	T R A	T C C	P R E	V V V	P	55
D E G L E C V P T	E E S N I	T M Q	I M R	I K P	H Q G	Q H I	G E M S		121	
D D G L E C V P T	G Q H Q V	R M Q	I L M	I R	Y P S	S Q L	G E M S		115	
R Q E N P	· · · · ·	· · · · ·	· · · · ·	· · · · ·	· · · · ·	· · · · ·	· · · · ·	· · · · ·	170	
R P Q P R S V P G W D S A	P G A	P S P A D I T H	P T P A P G P L						177	
R C K A R	Q L E L N	E R T C R C D	K P R R						191	
R C Q G R	L E L N	P D T C R C R	K L R R						222	

Fig 6 (iii)

Fig. 6 (iii)

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Areas of 100% homology are boxed and conserved residues thought to be involved in homodimerisation are underlined. The VEGF sequence depicted includes the 26 amino acid leader sequence (removal of which gives rise to mature VEGF₁₆₅) giving a total length of 191 amino acids.

Homology of SOM175 to VEGF₁₆₅ is 27% (33%) at the protein level, however within this are blocks of 100% homology. In particular, many structural residues are conserved including those thought to be involved in homodimerisation of VEGF (by comparison with PDGF).

ie. Cysteine-47

Proline-70, Cysteine-72, Valine-74

Arginine-77, Cystein-78, Glycine-80, Cysteines-81 & 82

Cysteine-89, Proline-91

Cysteines 122 & 124

Fig.6(iii)

SPLICE VARIANTS OF SOM175

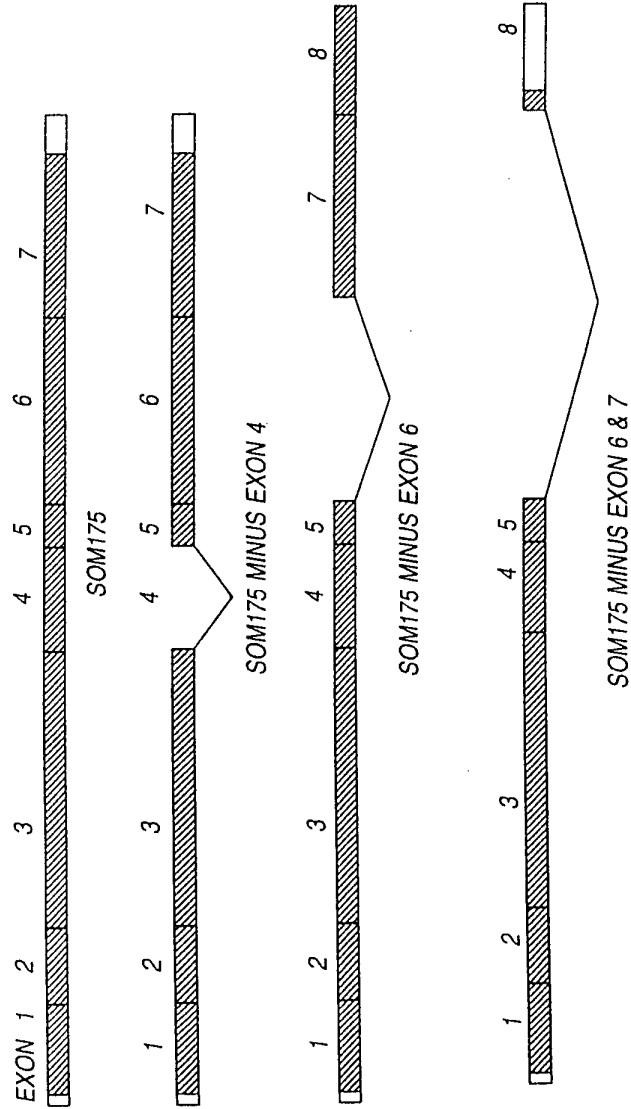
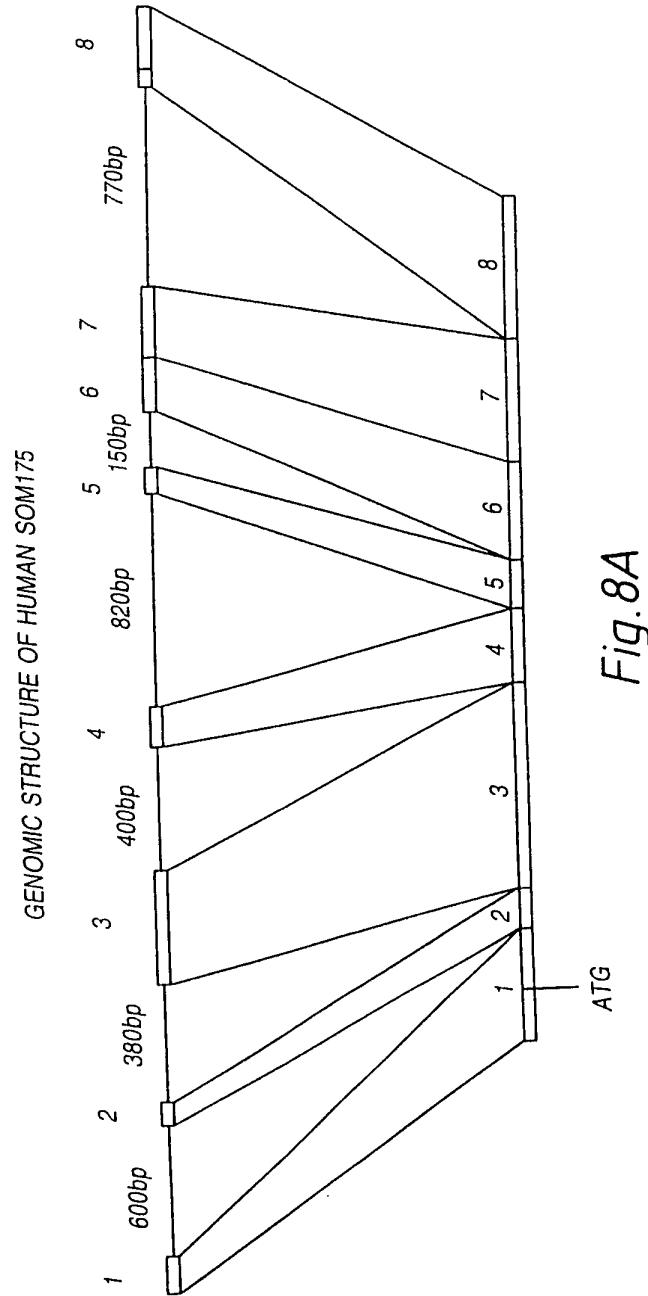


Fig.7

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5'UTR...	ATGAGG	*Exon 1 (60bp)	GGCCAG	gtacgtgagg
tctccacacag	GCCCTT	Exon 2 (43bp)	GGAAAG	aatacttaca
tctgctccca	TGGTGT	Exon 3 (187bp)	ATGCAG	gtccgagatg
ctgaatacacag	ATCCTC	Exon 4 (73bp)	ATGCAG	gtgtcaggca
acttttcaag	ACCTAA	Exon 5 (34bp)	AGACAG	gtgagtctttt
ctcctccgta	GGCTGC	Exon 6 (101bp)	CTCCAG	ccccaggccc
cccactccag	CCCCAG	Exon 7 (109bp)	ACCCAG	acacctgtag
ccctgctcag	GTGCCG	*Exon 8 (22bp)	AGGTGA	...3'UTR

Fig.8B

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36/52 <i>Fig. 9(i)</i>	37/52 <i>Fig. 9(ii)</i>
38/52 <i>Fig. 9(iii)</i>	39/52 <i>Fig. 9(iv)</i>

Fig. 9

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-163 gcacgagctcaggccgctcgctgcggcgctg
-103 gggggccgcggaggagccgccccctgcgcc
-43 ggcggtctctggctgacccccccccacaccg

16 CGTCGCCTGCTGCTTGTGCACTGCTGCAG
R R L L L V A L L Q

76 TTTGATGGCCCCAGTCACCAGAAGAAAGTG
F D G P S H Q K K V

136 ACATGCCAGCCCAGGGAGGTGGTGGTGCCT
T C Q P R E V V V P

196 AAACAACTAGTGCCCAGCTGTGTGACTGTG
K Q L V P S C V T V

256 GGCCTGGAATGTGTGCCCACTGGGCAACAC
G L E C V P T G Q H

316 TACCCGAGCAGTCAGCTGGGGGAGATGTCC
Y P S S Q L G E M S

376 CCTAAAAAAGGAGAGTGCTGTGAGGCCA
P K K K E S A V R P

436 CAGCCCCGCTCTGTTCCGGGCTGGGACTCT
Q P R S V P G W D S

Fig 9(i)

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cgttgcgctgcctgcgcccagggctcggga
ccgccccgggtccccgggtccgcgccatgg
ccgggctagggcccgATGAGCCCCCTGCTG
M S P L L -17
CTGGCTCGCACCCAGGCCCTGTGTCCCAG
L A R T Q A P V S Q 4
GTGCCATGGATAGACGTTTATGCACGTGCC
V P W I D V Y A R A 24
CTGAGCATGGAACATCATGGGCAATGTGGTC
L S M E L M G N V V 44
CAGCGCTGTGGTGGCTGCTGCCCTGACGAT
Q R C G G C C P D D 64
CAAGTCCGAATGCAGATCCTCATGATCCAG
Q V R M Q I L M I Q 84
CTGGGAGAACACAGCCAATGTGAATGCAGA
L G E H S Q C E C R 104
GACAGGGTTGCCATACCCCACCACCGTCCC
D R V A I P H H R P 124
ACCCCGGGAGCACCCCTCCCCAGCTGACATC
T P G A P S P A D I 144

Fig.9(ii)

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496 ATCCATCCCACTCCAGCCCCAGGATCCTCT
I H P T P A P G S S
S P R I L

556 CTGACCCCCGGACCTGCCGTTGCCGCTGTA
L T P G P A V A A V
P D P R T C R C R C

616 GGGGCTTAGAGCTCAACCCAGACACCTGTA
G A *
R G L E L N P D T C

676 ctttccagactccacgggcccggctgcttt
736 agcacaggcgtaacctcctcagtcctgggag
796 gagctctctcgcctatcttttatctcccaga
856 atgtctcacctcaggggccagggtactctc
916 ttctggctggctgtctcccctcactatgaa
976 gggttctgttatgataactgtgacacacac
1036 gacactaaaaaaaaaaaaaaaaaaaaaaaa

Fig.9(iii)

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GCCCGCCTTGCACCCAGCGCCGCCAACGCC
A R L A P S A A N A 164
C P P C T Q R R Q R 130

GACGCCGCGCTTCCTCCATTGCCAAGGGC
D A A A S S I A K G 184
R R R R F L H C Q G 150

↓
GGTGCCGGAAGCCGCGAAAGTGAcaagctg 186
R C R K P R K * 167

tatggccctgcttcacagggagaagagtgg
gtcactgccccaggacctggaccttttaga
gctgccatctaacaattgtcaaggaacctc
tcaacttaaccaccctgggtcaagtgagcatc
aaccccaaacttctaccaataacgggattt
acacactcacactctgataaaagagatgga
aaaaaaaaaaaa

Fig.9(iv)

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Fig 10(i)	Fig 10(ii)

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A

hVRF167	-21	MSPLLRRLLLAALLQLAPAQAP	↓
mVRF167	-21	MSPLLRRLLLVALLQLARTQAP	
hVRF167	30	EVVVPLTVELMGTVAQLVPSC	
		:	
mVRF167	30	EVVVPLSMELMGNVVKQLVPSC	
hVRF167	80	ILMIRYPSSQLGEMSLEEHSQC	
		:	
mVRF167	80	ILMIQYPSSQLGEMSLGEHSQC	
hVRF167	130	RPDPRTCRCRCRRRSFLRCQGR	
		:	
mVRF167	130	RPDPRTCRCRCRRRFLHCQGR	

B

hVRF186	116	RAATPHHRPQPRSVPGWDSAPG
mVRF186	116	RVAIPHHRPQPRSVPGWDSTPG
hVRF186	166	TPGPAAAAADAAASSVAKGGA*
		:
mVRF186	166	TPGPAVAAVDAAASSIAKGGA*

Fig.10(i)

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VSQPDAPGHQRKVVSWIDVYTRATCQPR 29
 ||| |:|:|:| | | | | | | | | |
 VSQFDGPSHQKKVVPWIDVYARATCQPR 29
 VTVQRCGGCCPDDGLECVPTGQHQVRMQ 79
 ||| | | | | | | | | | | | | | | | | | |
 VTVQRCGGCCPDDGLECVPTGQHQVRMQ 79
 ECRPKKKDSAVKPDSPRPLCPRCTQHHQ 129
 ||| | | |:| |:| | | | | | | | |:|
 ECRPKKESAVRPDSPRILCPPCTQRRQ 129
 GLELNPDTCRCKLRR* 167
 ||| | | | | | | | | | | | | | | | | | |
 GLELNPDTCRCKPRK* 167
 APSPADITHPTPAPGPSAHAAPSTTSAL 165
 ||| | | | | | | | | | | | | | | | | | |
 APSPADIIHPTPAPGSSARLAPSAANAL 165
 186
 186

Fig.10(ii)

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Fig 11(i)	Fig 11(ii)

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mVRF167	-21	MSPLLRRL..LLVALLQL..
		: :
mVEGF188	-26	MNFLLSWVHWTLALLLYLHH
mVRF167	25	TCQPREVVVPLSMELMGNVV
		: : : :
mVEGF188	24	YCRPIETLVDIFQEYPDEIE
mVRF167	75	QVRMQILMIQYPSSQ.LGEM
		: : :
mVEGF188	74	NITMQIMRIKPHQSQHIGEM
mVRF167	119ILCPPC
		:
mVEGF188	124	QKRKRKKS RFKSWSVHCEPC
mVRF167	152	GLELNPDTCRCKPRK
		:
mVEGF188	173	QLELNERTCRCDKPRR

Fig.11(i)

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AR.TQAPVSQFDGPSHQKKVVPWIDVYARA	24
: : : : : : ::	
AKWSQAAPT.T.EGEQKSHEVIKFMDVYQRS	23
KQLVPSCVTVQRCGGCCPDDGLECVPTGQH	74
: : : :: ::	
YIFKPSCVPLMRCAGCCNDEALECVPTSES	73
SLGEHSQCECRPKKESAVRPDSPR.....	118
: :	
SFLQHSRCECRPKKDRTPKPKSVRGKGKG	123
TQRRQR...PDPRTCRCRCRRRFLHCQGR	151
: : : : : :	
SERRKHLFVQDPQTCKCCKNTDS.RCKAR	172
	167
	188

Fig.11(ii)

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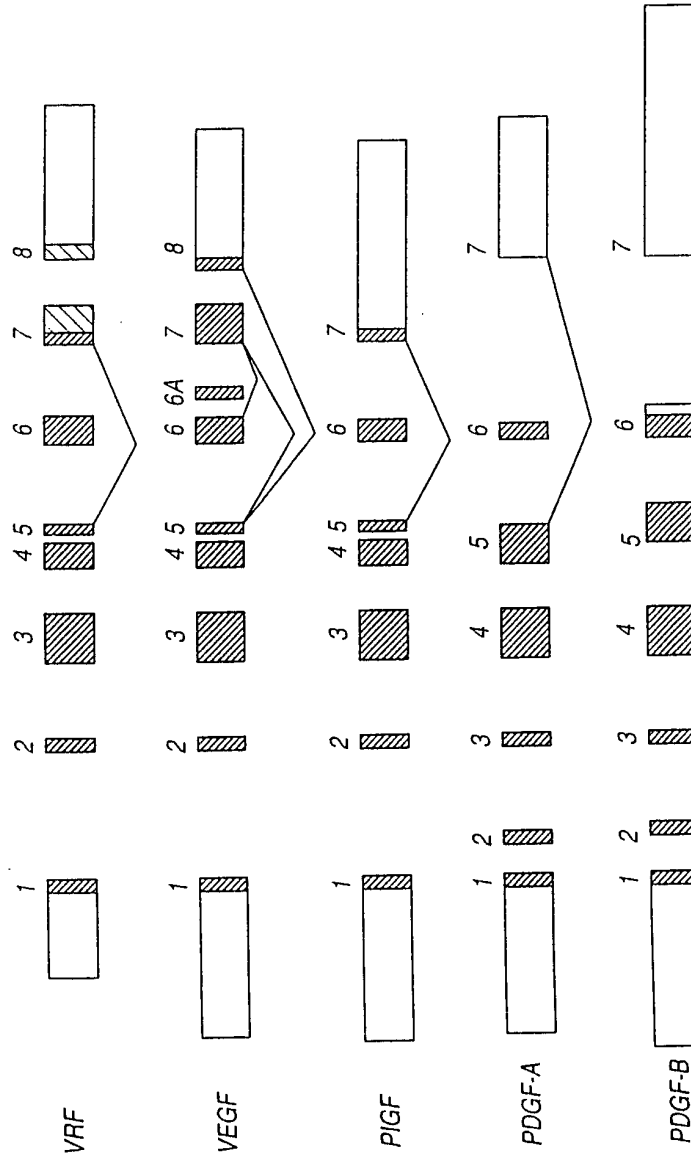


Fig.12

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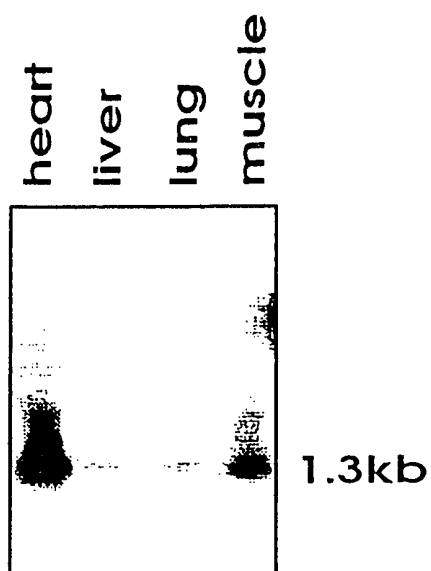


Fig.13

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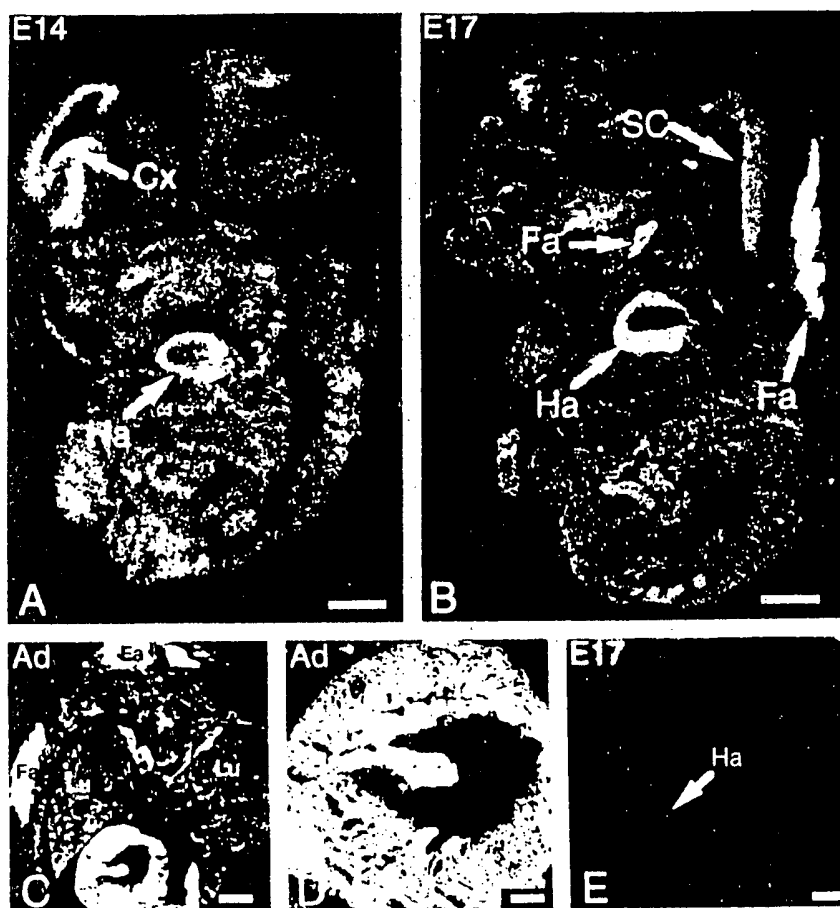


Fig.14

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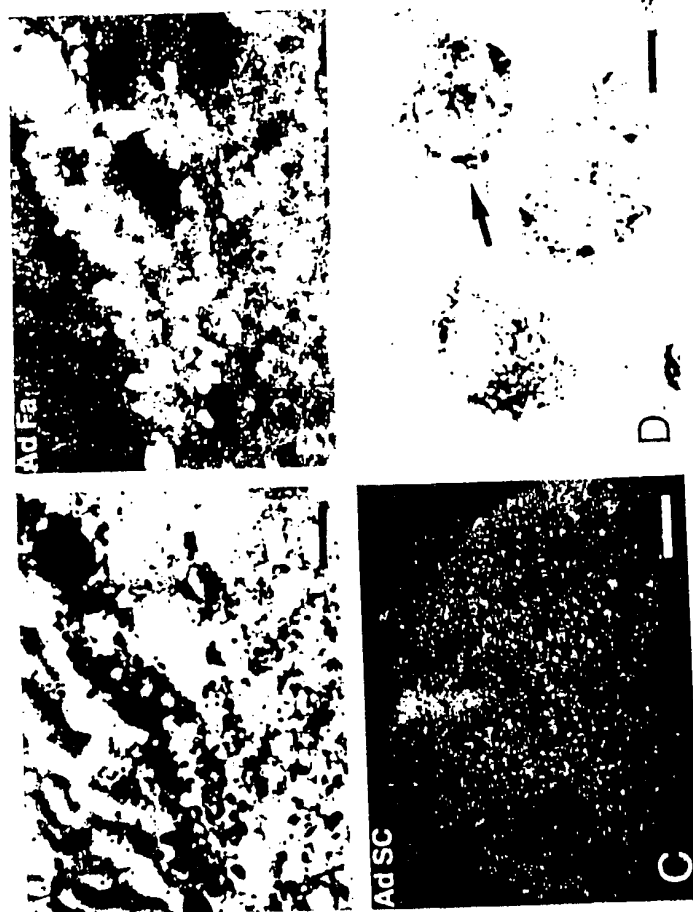


Fig.15

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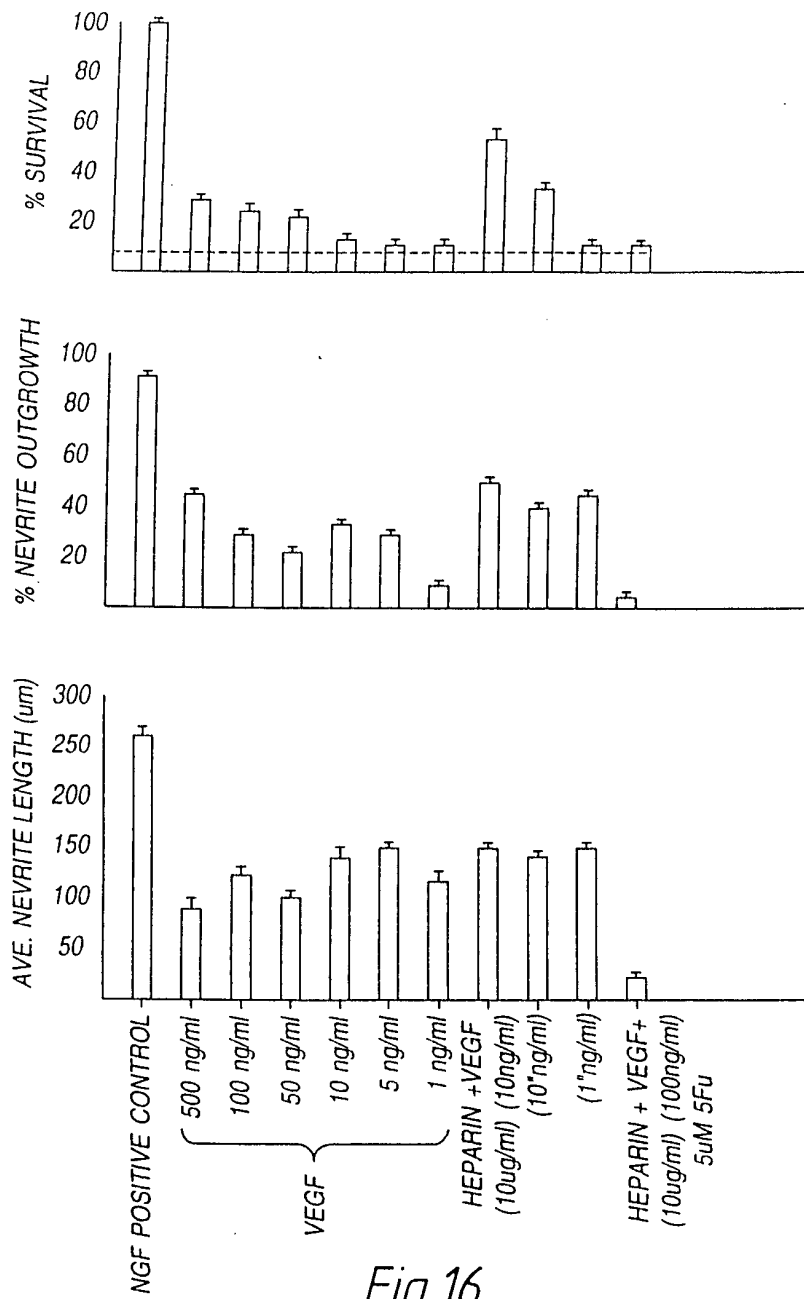


Fig.16

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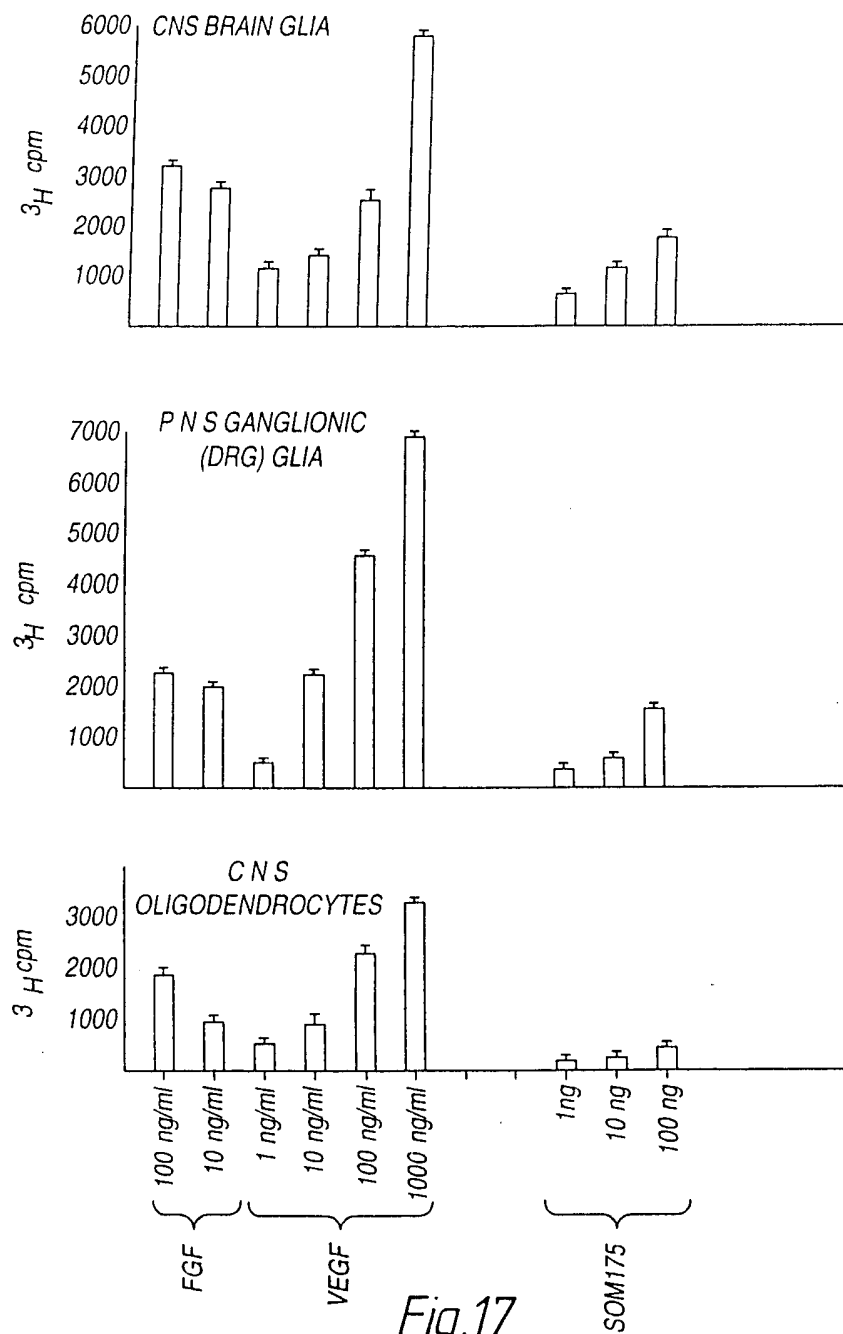


Fig.17

MOUSE ASTROGLIAL CELLS

